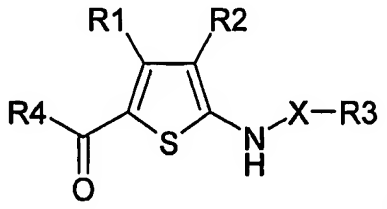
CLAIMS

1. The use of a compound for the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by a p38 MAP kinase; the compound being defined by formula (I):



(I)

wherein:

R^1 and R^2 are the same or different and each is selected from hydrogen, C_{1-4} hydrocarbyl, halogen and cyano;

X is selected from C=O, C=S, C(=O)NH, C(=S)NH, C(=O)O, C(=O)S, C(=S)O and C(=S)S;

R^3 is selected from aryl and heteroaryl groups each having from 5 to 12 ring members, the aryl and heteroaryl groups each being unsubstituted or substituted by one or more substituent groups R^7 selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, carbocyclic and heterocyclic groups having from 3 to 12 ring members; a group R^a-R^b wherein R^a is a bond, O, CO, $X^1C(X^2)$, $C(X^2)X^1$, $X^1C(X^2)X^1$, S, SO, SO_2, NR^c, SO_2NR^c or NR^cSO_2; and R^b is selected from hydrogen, carbocyclic and heterocyclic groups having from 3 to 7 ring members, and a C_{1-8} hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, amino, mono- or di-C_{1-4} hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the C_{1-8} hydrocarbyl group may optionally be replaced by O, S, SO, SO_2, NR^c, $X^1C(X^2)$, $C(X^2)X^1$ or $X^1C(X^2)X^1$;

X^1 is O, S or NR^c and X^2 is =O, =S or =NR^c;

R^c is hydrogen or C_{1-4} hydrocarbyl;

R^4 is a group YR^5 or a group R^6;

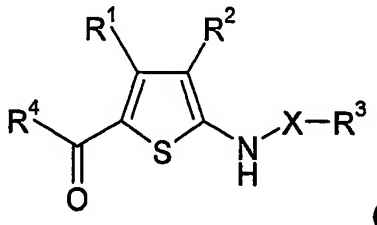
Y is is NH, O or S;

R^5 is selected from (a) carbocyclic and heterocyclic groups having from 3 to 12 ring members; and (b) C_{1-8} hydrocarbyl groups optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, amino, mono- or di-C_{1-4} hydrocarbylamino, and carbocyclic and heterocyclic groups having from 3 to 12 ring members, wherein one or more carbon atoms of the C_{1-8} hydrocarbyl group may optionally be replaced by O, S, SO, SO_2, NR^c, $X^1C(X^2)$, $C(X^2)X^1$ or $X^1C(X^2)X^1$, provided that when Y is O, a carbon atom adjacent to the group Y is not replaced by O; and

R^6 is a heterocyclic group having from 4 to 12 ring members and containing at least one ring nitrogen atom through which R^6 is linked to the adjacent carbonyl group;

wherein the carbocyclic and heterocyclic groups of substituents R^5 and R^6 are each unsubstituted or substituted by one or more substituent groups R^7 as hereinbefore defined.

2. A compound of the formula (Ia):



(Ia)

wherein:

R^1 and R^2 are the same or different and each is selected from hydrogen, C_{1-4} hydrocarbyl, halogen and cyano;

X is selected from C=O, C=S, C(=O)NH, C(=S)NH, C(=O)O, C(=O)S, C(=S)O and C(=S)S;

R^3 is selected from aryl and heteroaryl groups each having from 5 to 12 ring members, the aryl and heteroaryl groups each being unsubstituted or substituted by one or more substituent groups R^7 selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, carbocyclic and

heterocyclic groups having from 3 to 12 ring members; a group R^a-R^b wherein R^a is a bond, O, CO, $X^1C(X^2)$, $C(X^2)X^1$, $X^1C(X^2)X^1$, S, SO, SO_2, NR^c, SO_2NR^c or NR^cSO_2; and R^b is selected from hydrogen, carbocyclic and heterocyclic groups having from 3 to 12 ring members, and a C_{1-8} hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, amino, mono- or di-C_{1-4} hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the C_{1-8} hydrocarbyl group may optionally be replaced by O, S, SO, SO_2, NR^c, $X^1C(X^2)$, $C(X^2)X^1$ or $X^1C(X^2)X^1$;

X^1 is O, S or NR^c and X^2 is =O, =S or =NR^c;

R^c is hydrogen or C_{1-4} hydrocarbyl;

R^4 is a group YR^5 or a group R^6;

Y is is NH, O or S;

R^5 is selected from (a) carbocyclic and heterocyclic groups having from 3 to 12 ring members; and (b) C_{1-8} hydrocarbyl groups optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, amino, mono- or di-C_{1-4} hydrocarbylamino, and carbocyclic and heterocyclic groups having from 3 to 12 ring members, wherein one or more carbon atoms of the C_{1-8} hydrocarbyl group may optionally be replaced by O, S, SO, SO_2, NR^c, $X^1C(X^2)$, $C(X^2)X^1$ or $X^1C(X^2)X^1$, provided that when Y is O, a carbon atom adjacent to the group Y is not replaced by O; and

R^6 is a heterocyclic group having from 4 to 12 ring members and containing at least one ring nitrogen atom through which R^6 is linked to the adjacent carbonyl group, provided that R^6 is other than a bicyclic group comprising a benzene ring fused to a 7-membered heterocyclic ring;

wherein the carbocyclic and heterocyclic groups of substituents R^5 and R^6 are each unsubstituted or substituted by one or more substituent groups R^7 as hereinbefore defined;

provided that:

(a) when X is C=O and R^3 is a heteroaryl group substituted by the group R^a-R^b where R^a is $NR^cC=O$, then R^b is other than an optionally further substituted phenyl, pyridyl or pyrimidinyl group having a carbocyclic or heterocylic group bonded to the *ortho* position thereof either directly or through an intervening linker atom or group of 1 or 2 atoms in length;

(b) when X is C=O, R^3 is other than:

(i) an optionally further substituted phenyl, pyridyl or pyrimidinyl group having a carbocyclic or heterocylic group bonded to the *ortho* position thereof either directly or through an intervening linker atom or group of 1 or 2 atoms in length;

(ii) a phenyl group having an oxy-substituent bonded to the *ortho* position thereof;

(iii) an optionally N-substituted pyrrolidine ring substituted on a carbon atom thereof by a group selected from thiol, substituted thiol, thiocarbonate and groups containing a β-lactam ring;

(c) when X is C=O and R^3 is an unsubstituted phenyl group, or a phenyl group substituted by one or more substituents, none of which are cyclic, then R^4 is other than alkoxy;

(d) when X is C(=O)NH and R^3 is a thiophene group bearing a 5-alkoxycarbonyl group, then R^4 is other than alkoxy;

(e) when Y is NH or O and R^5 is a C_{2-4} alkylene group bearing a terminal amino, monoalkylamino or dialkylamino substituent, wherein the alkyl moieties of the mono-and dialkylamino substituents are themselves unsubstituted or further substituted; then X-R^3 is other than an unsubstituted or substituted benzoyl group;

(f) when Y is NH and R^5 is a C_{1-3} alkylene group bearing a terminal carboxy or alkoxycarbonyl substituent; then X-R^3 is other than a 4-carbamimidoyl-benzoyl group;

(g) when X is C=O, Y is NH and R^5 is a 3-dimethylaminoprop-1-yl group; then R^3 is other than a 5-nitro-2-thiophenyl group; and

(h) when X is C=O, R^4 is ethoxy, R^1 is methyl and R^2 is hydrogen or cyano; then R^3 is other than an unsubstituted phenyl group.

3. A compound according to claim 2 wherein R^3 is a monocyclic aryl or heteroaryl group.

4. A compound according to claim 2 wherein R^3 is selected from phenyl, indenyl, tetrahydronaphthyl, naphthyl, pyridyl, pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, oxadiazolyl, oxatriazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiadiazolyl (e.g. [1,3,4]-thiadiazolyl), pyrazolyl, pyrazinyl, pyrimidinyl, triazinyl, quinolinyl, isoquinolinyl, tetrazolyl, benzfuranyl, chromanyl, thiochromanyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzthiazolyl and benzisothiazolyl, isobenzofuranyl, isoindolyl, indolizinyl, indolinyl, isoindolinyl, purinyl (e.g., adenine, guanine), indazolyl, benzodioxolyl, chromenyl, isochromenyl, chroman, isochromanyl, benzodioxanyl, quinolizinyl, benzoxazinyl, benzodiazinyl, pyridopyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, phthalazinyl, naphthyridinyl and pteridinyl, each being optionally substituted by one or more substituent groups R^7.

5. A compound according to claim 3 wherein R^3 is a monocyclic aryl group.

6. A compound according to claim 3 wherein R^3 is a monocyclic heteroaryl group containing at least one nitrogen atom.

7. A compound according to claim 6 wherein the heteroaryl group is selected from pyrazolyl, and thiadiazolyl (e.g. [1,3,4]-thiadiazolyl).

8. A compound according to any one of claims 2 to 7 wherein the aryl group or heteroaryl group R^3 contains one or more substituent groups R^7 selected from halogen, carbocyclic and heterocyclic groups having from 4 to 7 ring members and optionally substituted C_{1-8} hydrocarbyl groups.

9. A compound according to claim 8 wherein the group R^3 contains a substituent R^7 which is selected from carbocyclic and heterocyclic groups having from 4 to 7 ring members.

10. A compound according to claim 9 wherein the carbocyclic or heterocyclic group is linked to the aryl or heteroaryl ring via a carbon nitrogen bond.

11. A compound according to claim 10 wherein the substituent group R^7 is a 4 to 7 membered (more typically 5 to 6 membered) heterocyclic group R^8 containing at least one nitrogen atom.

12. A compound according to claim 11 wherein R^8 is selected from morpholino, piperidino, piperazino, N-methyl piperazino and pyrrolidino.

13. A compound according to claim 11 wherein R^8 is morpholino.

14. A compound according to any one of the preceding claims wherein R^3 is a phenyl group bearing one or two *meta* substituents.

15. A compound according to claim 14 wherein one *meta* position on the phenyl ring is unsubstituted or is substituted by a group selected from fluorine, chorine, methoxy, trifluoromethoxy, trifluoromethyl, ethyl, methyl and isopropyl; and the other *meta* position is substituted by a group selected from fluorine, chorine, methoxy, trifluoromethoxy, trifluoromethyl, ethyl, methyl, isopropyl, isobutyl, t-butyl, phenyl, substituted phenyl, and five and six membered monocyclic heterocyclic groups.

16. A compound according to claim 15 wherein both *meta* positions on the phenyl ring are substituted, one substituent being a halogen, preferably fluoro, and the other substituent being a group R^8 as defined in any one of claims 11 to 13.

17. A compound according to claim 8 wherein R^3 is a pyrazole group substituted by two substituent groups R^7.

18. A compound according to claim 17 wherein the two substituent groups R^7 are located on non-adjacent ring members.

19. A compound according to claim 17 or claim 18 wherein at least one of the substituents is located at a position *meta* or β with respect to the ring member linked to the group X.

20. A compound according to any one of claims 17 to 19 wherein the pyrazole group ring is substituted by an optionally substituted phenyl group (e.g. 4-fluorophenyl) and a C_{1-4} hydrocarbyl group (e.g. *tert*-butyl).

21. A compound according to any one of claims 2 to 20 wherein X is selected from C=O and C(=O)NH.

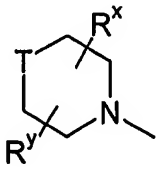
22. A compound according to claim 21 wherein X is C=O.

23. A compound according to claim 21 wherein X is C(=O)NH.

24. A compound according to any one of claims 2 to 23 wherein R^4 is a group R^6 as defined in any one of the preceding claims.

25. A compound according to claim 24 wherein R^6 is a monocyclic group having from 4 to 7 ring members.

26. A compound according to claim 25 wherein the monocyclic group R^6 is a group:



where T is N-methyl or O; R^x and R^y are the same or different and are selected from hydrogen and methyl; or one of R^x and R^y is selected from hydroxymethyl and ethyl and the other is hydrogen.

27. A compound according to clam 26 wherein T is O and R^x and R^y are both hydrogen.

28. A compound according to claim 25 wherein the monocyclic group is selected from piperidine, piperazine, N-methylpiperazine, morpholine, pyrrolidine, imidazoline, imidazolidine, thiazolidine and oxazolidine.

29. A compound according to claim 28 wherein the monocyclic group is selected from morpholine, piperidine, piperazine and N-methyl piperazine.

30. A compound according to any one of claims 2 to 23 wherein R^4 is a group YR^5 as defined in any one of the preceding claims.

31. A compound according to claim 30 wherein Y is NH or O.

32. A compound according to claim 31 wherein Y is NH.

33. A compound according to claim 32 wherein Y is O.

34. A compound according to any one of claims 30 to 33 wherein R^5 is a C_{1-8} hydrocarbyl group substituted by a carbocyclic or heterocylic group.

35. A compound according to claim 34 wherein the substituted hydrocarbyl group is an alkyl group of up to 4 carbon atoms (more usually up to 3 carbon atoms, for example up to 2 carbon atoms, preferably 1 carbon atom).

36. A compound according to claim 35 wherein the substituted hydrocarbyl group is selected from arylmethyl, arylethyl, heteroarylmethyl and heteroarylethyl groups.

37. A compound according to claim 36 wherein the substituted hydrocarbyl group is a pyridylmethyl group.

38. A compound according to any one of claims 30 to 33 wherein R^5 is a carbocylic or heterocyclic group.

39. A compound according to claim 38 wherein the carbocylic or heterocyclic group are aromatic.

40. A compound according to claim 39 wherein R^5 is a phenyl group optionally substituted by one or more substituents R^7.

41. A compound according to claim 40 wherein the phenyl group is substituted by one or more substituents (preferably one) selected from, C_{1-4} hydrocarbyl, halogen (e.g. fluoro and chloro), hydroxy, trifluoromethyl and cyano.

42. A compound according to claim 41 wherein the phenyl group bears a fluoro (e.g. 4-fluoro) substituent.

43. A compound according to claim 39 wherein R^5 is a monocyclic aromatic heterocyclic (heteroaryl) group containing one or two nitrogen ring members.

44. A compound according to any one of claims 30 to 33 wherein R^5 is a C_{1-8} hydrocarbyl group such as an alkyl group, e.g. methyl or ethyl.

45. A compound according to any one of claims 2 to 44 wherein R^2 is cyano and R^4 is other than C_{1-6} alkoxy, phenoxy, benzyloxy and C_{1-6} alkylamino.

46. A compound according to any one of claims 2 to 45 wherein R^2 is selected from hydrogen, C_{1-4} hydrocarbyl and halogen (e.g. chlorine and fluorine).

47. A compound according to any one of claims 2 to 46 wherein R^1 is selected from hydrogen, C_{1-4} hydrocarbyl and halogen (e.g. chlorine and fluorine).

48. A compound according to claim 47 wherein R^1 is a halogen, preferably chlorine.

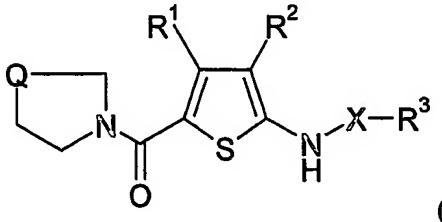
49. A compound according to any one of claims 2 to 48 wherein the total number of carbon, halogen and nitrogen atoms making up the substituent groups R^1 and R^2 does not exceed 5.

50. A compound according to claim 49 wherein the total number of carbon, halogen and nitrogen atoms making up the substituent groups R^1 and R^2 is in the range 0 to 4, for example 0, 1, 2, or 3.

51. A compound according to any one of claims 2 to 50 containing a combination of groups R^1 and R^2 selected from: (a) R^1 = chlorine & R^2 = methyl; (b) R^1 = chlorine & R^2 = hydrogen; (c) R^1 = hydrogen & R^2 = hydrogen; (d) R^1 = methyl & R^2 = hydrogen; (e) R^1 = cyano & R^2 = methyl; and (f) R^1 = methyl & R^2 = cyano.

52. A compound according to claim 51 wherein the combination of groups R^1 and R^2 is selected from combinations (a) and (c).

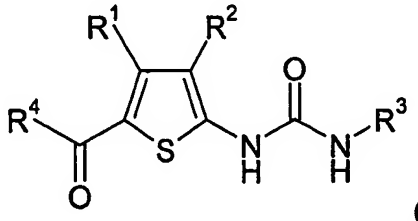
53. A compound of the formula (II);



(II)

wherein R^1, R^2 and R^3 are as hereinbefore defined in any one of the preceding claims, and Q is selected from CH_2, OCH_2, $NHCH_2$, $N(CH_3)CH_2$ or CH_2CH_2.

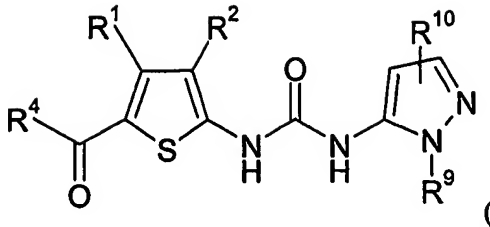
54. A compound of the formula (III):



(III)

wherein R^1 to R^4 are as defined in any one of claims 1 to 52.

55. A compound of the formula (IVa):



(IVa)

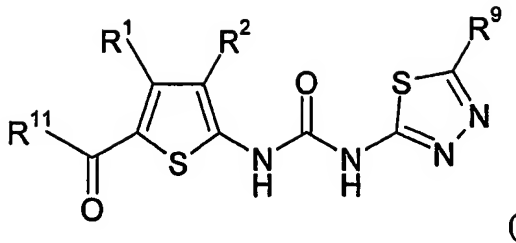
wherein R^1, R^2 and R^4 are as defined in any one of claims 1 to 52;

R^9 is selected from carbocyclic and heterocyclic groups having from 3 to 7 ring members; a group R^e-R^f wherein R^e is a bond, CO, $X^1C(X^2)$, $C(X^2)X^1$, $X^1C(X^2)X^1$, SO, SO_2, SO_2NR^c or NR^cSO_2; and R^f is selected from (a) hydrogen, (b) carbocyclic and heterocyclic groups having from 3 to 7 ring members, and (c) a C_{1-8} hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, amino, mono- or di-C_{1-4} hydrocarbylamino, and carbocyclic and heterocyclic groups having from 3 to 7 ring members and wherein one or more carbon atoms of the C_{1-8} hydrocarbyl group may optionally be replaced by O, S, SO, SO_2, NR^c, $X^1C(X^2)$, $C(X^2)X^1$ or $X^1C(X^2)X^1$; and

R^{10} is selected from hydrogen, halogen and C_{1-6} hydrocarbyl optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, and wherein one or more carbon atoms of the C_{1-6} hydrocarbyl group may optionally be replaced by O, S, SO, SO_2, NR^c, $X^1C(X^2)$, $C(X^2)X^1$ or $X^1C(X^2)X^1$; where X^1, X^2 and R^c are as defined in claim 1.

56. A compound according to claim 55 wherein R^9 is a phenyl group, for example a fluorophenyl group (e.g. a 4-fluorophenyl group); and R^{10} is a hydrogen atom or a C_{1-6} alkyl group such as a tertiary butyl group.

57. A compound of the formula (IVb):



(IVb)

wherein R^{11} is R^6 or NHR^5; and R^1, R^2, R^5, R^6 and R^9 are as defined in any one of the preceding claims.

58. A compound according to any one of claims 2 to 57 wherein R^3 is selected from the groups set out in Table 1 herein.

59. A compound according to claim 2 selected from:

3-chloro-5-(3-fluoro-5-morpholin-4-yl-benzoylamino)-4-methyl-thiophene-2-carboxylic acid methyl ester;

N-[4-chloro-3-methyl-5-(morpholine-4-carbonyl)-thiophen-2-yl]-3-fluoro-5-morpholin-4-yl-benzamide;

5-{3-[5-tert-butyl-2-(4-fluoro-phenyl)-2H-pyrazol-3-yl]-ureido}-3-chloro-4-methyl-thiophene-2-carboxylic acid methyl ester;

1-[5-tert-butyl-2-(4-fluoro-phenyl)-2H-pyrazol-3-yl]-3-[4-chloro-3-methyl-5-(morpholine-4-carbonyl)-thiophen-2-yl]-urea;

5-(3-fluoro-5-morpholin-4-yl-benzoylamino)-3-methyl-thiophene-2-carboxylic acid ethyl ester;

3-fluoro-N-[4-methyl-5-(morpholin-4-carbonyl)-thiophen-2-yl]-5-morpholin-4-yl-benzamide;

5-{3-[5-tert-butyl-2-(4-fluoro-phenyl)-2H-pyrazol-3-yl]-ureido}-thiophene-2-carboxylic acid ethyl ester;

1-[5-tert-butyl-2-(4-fluorophenyl)-2H-pyrazol-3-yl]-3-[5-(morpholine-4-carbonyl)-thiophen-2-yl]-urea;

5-{3-[5-tert-butyl-2-(4-fluoro-phenyl)-2H-pyrazol-3-yl]-ureido}-3-methyl-4-cyano-thiophene-2-carboxylic acid methyl ester;

3-cyano-5-(4-fluorobenzoylamino)-4-methyl-thiophene-2-carboxylic acid methyl ester;

N-[4-chloro-3-methyl-5-(morpholine-4-carbonyl)-thiophen-2-yl]-4-fluorobenzamide;

N-[4-chloro-3-methyl-5-(4-fluoro-phenylaminocarbonyl)-thiophen-2-yl]-4-fluorobenzamide;

3-chloro-5-(4-fluorobenzoylamino)-4-methyl-thiophene-2-carboxylic acid methyl ester;

1-[5-tert-butyl-2-(4-fluoro-phenyl)-2H-pyrazol-3-yl]-3-[4-chloro-3-methyl-5-(1-methylpiperazine-4-carbonyl)-thiophen-2-yl]-urea;

1-[5-tert-butyl-2-(4-fluoro-phenyl)-2H-pyrazol-3-yl]-3-[4-chloro-3-methyl-5-(4-pyridylmethylaminocarbonyl)-thiophen-2-yl]-urea;

N-[4-chloro-3-methyl-5-(4-pyridylmethylaminocarbonyl)-thiophen-2-yl]-3-fluoro-5-morpholin-4-yl-benzamide;

N-[4-chloro-3-methyl-5-(2,3,5-trimethyl-2H-pyrazol-4-ylaminocarbonyl)-thiophen-2-yl]-3-fluoro-5-morpholin-4-yl-benzamide;

N-[4-chloro-3-methyl-5-(4-fluorophenylaminocarbonyl)-thiophen-2-yl]-3-fluoro-5-morpholin-4-yl-benzamide;

N-[4-chloro-3-methyl-5-(1-methylpiperazin-4-ylaminocarbonyl)-thiophen-2-yl]-3-fluoro-5-morpholin-4-yl-benzamide;

N-[4-chloro-3-methyl-5-(2-amino-pyrimidin-5-ylaminocarbonyl)-thiophen-2-yl]-3-fluoro-5-morpholin-4-yl-benzamide;

1-[2-(tetrahydrofuran-2-yl)-thiadiazol-5-yl]-3-[4-chloro-3-methyl-5-(morpholine-4-carbonyl)-thiophen-2-yl]-urea;

1-[4-chloro-3-methyl-5-(morpholine-4-carbonyl)-thiophen-2-yl]-3-[5-cyclohexyl- [1,3,4]thiadiazol-2-yl]-urea;

1-[4-chloro-3-methyl-5-(morpholine-4-carbonyl)-thiophen-2-yl]-3-(5-morpholin-4-yl-[1,3,4]thiadiazol-2-yl)-urea;

1-[4-chloro-3-methyl-5-(morpholine-4-carbonyl)-thiophen-2-yl]-3-[5-(4-methyl-piperazin-1-yl)-[1,3,4]thiadiazol-2-yl]-urea; and

1-[5-tert-Butyl-2-(2,4-difluoro-phenyl)-2H-pyrazol-3-yl]-3-[4-chloro-3-methyl-5-(morpholine-4-carbonyl)-thiophen-2-yl]-urea.

60. A compound according to any one of claims 2 to 59 in the form of a salt, solvate or N-oxide.

61. The use according to claim 1 wherein the compound of the formula (I) is in the form of a salt, solvate or N-oxide.

62. A compound as defined in any one of claims 2 to 60 for use in the prophylaxis or treatment of a disease state or condition mediated by a p38 MAP kinase.

63. The use of a compound as defined in any one of claims 2 to 60 for the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by a p38 MAP kinase.

64. A method for the prophylaxis or treatment of a disease state or condition mediated by a p38 MAP kinase, which method comprises administering to a subject (e.g. a human subject) in need thereof a compound as defined in any one of claims 1 to 61.

65. A method of inhibiting a p38 MAP kinase, which method comprises contacting the p38 MAP kinase with a kinase-inhibiting compound as defined in any one of claims 1 to 61.

66. A method of modulating a cellular process by inhibiting the activity of a p38 MAP kinase using a compound as defined in any one of claims 1 to 61, which method comprises bringing the compound of formula (I) into contact with a cellular environment containing the p38 MAP kinase.

67. A compound as defined in any one of claims 2 to 60 for use in medicine, for example for use in therapy.

68. A pharmaceutical composition comprising a compound as defined in any one of claims 2 to 60 together with a pharmaceutically acceptable carrier.

69. A compound for use, use or method as defined in any one of claims 1 and 61 to 64 wherein the disease state or condition mediated by a p38 MAP kinase is selected from rheumatoid arthritis, osteoarthritis, rheumatoid spondylitis, gouty arthritis, traumatic arthritis, rubella arthritis, psoriatic arthritis, and other arthritic conditions; Alzheimer's disease; toxic shock syndrome, the inflammatory reaction induced by endotoxin or inflammatory bowel disease; tuberculosis, atherosclerosis, muscle degeneration, Reiter's syndrome, gout, acute synovitis, sepsis, septic shock, endotoxic shock, gram negative sepsis, adult respiratory distress syndrome, cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcoisosis, bone resorption diseases, reperfusion injury, graft vs. host reaction, allograft rejections, fever and myalgias due to infection, such as influenza, cachexia, in particular cachexia secondary to infection or malignancy, cachexia secondary to acquired immune deficiency syndrome (AIDS), AIDS, ARC (AIDS related complex), keloid formation, scar tissue formation, Crohn's disease, ulcerative colitis, pyresis, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), asthma, pulmonary fibrosis and bacterial pneumonia.

70. The use of a compound as defined in any one of claims 1 to 61 for the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition selected from selected from rheumatoid arthritis, osteoarthritis, rheumatoid spondylitis, gouty arthritis, traumatic arthritis, rubella arthritis, psoriatic arthritis, and other arthritic conditions; Alzheimer's disease; toxic shock syndrome, the inflammatory reaction induced by endotoxin or inflammatory bowel disease; tuberculosis, atherosclerosis, muscle degeneration, Reiter's syndrome, gout, acute synovitis, sepsis, septic shock, endotoxic shock, gram negative sepsis, adult respiratory distress syndrome, cerebral malaria, chronic pulmonary

inflammatory disease, silicosis, pulmonary sarcoisosis, bone resorption diseases, reperfusion injury, graft vs. host reaction, allograft rejections, fever and myalgias due to infection, such as influenza, cachexia, in particular cachexia secondary to infection or malignancy, cachexia secondary to acquired immune deficiency syndrome (AIDS), AIDS, ARC (AIDS related complex), keloid formation, scar tissue formation, Crohn's disease, ulcerative colitis, pyresis, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), asthma, pulmonary fibrosis and bacterial pneumonia.

71. A method for the prophylaxis or treatment of a disease state or condition selected from the disease states defined in claim 70, which method comprises administering to a subject (e.g. a human subject) in need thereof a therapeutically effective amount of a compound as defined in any one of claims 1 to 61.

72. A compound for use, use or method as defined in any one of claims 1, 61 to 64 and 69 to 71 wherein the disease state is selected from inflammatory and arthritic diseases and conditions such as Reiter's syndrome, acute,synovitis, rheumatoid arthritis, osteoarthritis, rheumatoid spondylitis, gouty arthritis, traumatic arthritis, rubella arthritis, psoriatic arthritis, graft vs. host reaction and allograft rejections.

73. A compound for use, use or method as defined in claim 72 wherein the disease state or condition is selected from rheumatoid arthritis and osteoarthritis.

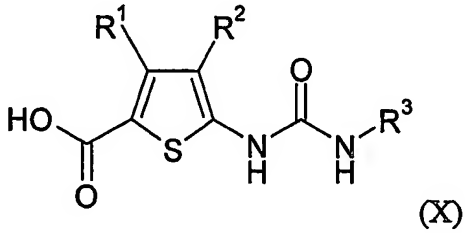
74. A compound for use, use or method as defined in any one of claims 1, 61 to 64 and 69 to 71 wherein the disease state is selected from chronic inflammatory lung diseases such as emphysema, chronic pulmonary inflammatory disease, chronic obstructive pulmonary disease (COPD), adult respiratory distress syndrome and acute respiratory distress syndrome (ARDS).

75. A compound for use, use or method as defined in claim 74 wherein the disease state is chronic obstructive pulmonary disease (COPD).

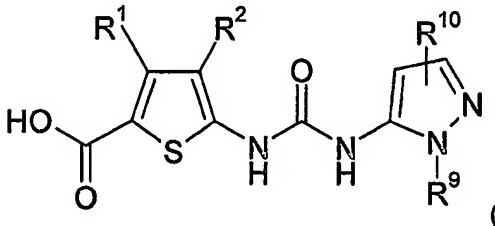
76. A pharmaceutical composition for administration by inhalation, the composition comprising a compound as defined in any one of claims 1 to 61 together with a pharmaceutically acceptable carrier.

77. A pharmaceutical composition according to claim 76 which is selected from inhalable dry powder compositions and aerosol compositions.

78. A compound selected from compounds of the formula (X) and (XI):



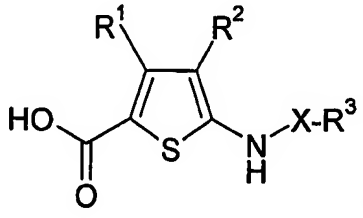
(X)



(XI)

wherein R^1, R^2, R^3, R^9 and R^{10} are as defined in any one of claims 2 to 60.

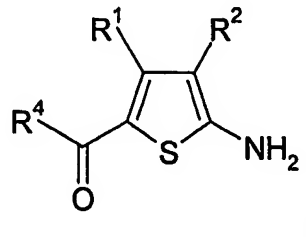
79. A process for the preparation of a compound as defined in any one of claims 2 to 60, which process comprises the reaction of a compound of the formula (V):



(V)

or an activated derivative thereof, with an amine, thiol or hydroxyl compound suitable for introducing the residue YR^5 or R^6.

80. A process for the preparation of a compound as defined in any one of claims 2 to 60, wherein X is C(=O)NH, which process comprises the reaction of a compound of the formula (X):



(X)

with phosgene and subsequently with a compound of the formula R^3NH_2.